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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/500,635	02/09/00	LEON	F 002076-033

000909
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HM12/0816

EXAMINER	
WILSON, M	
ART UNIT	PAPER NUMBER
1633	10

DATE MAILED: 08/16/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev.11/00)

1- File Copy

Office Action Summary	Application No.	Applicant(s)	
	09/500,635	LEON ET AL.	
	Examin r	Art Unit	
	Michael Wilson	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 May 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *11-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 18-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-20 are pending in the instant application.

Election/Restriction

Applicant's election without traverse of Group I, claims 1-10 and 18-20 in Paper No. 9 is acknowledged. Claims 11-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 9. Claims 1-10 and 18-20 are under consideration.

General Comment

The chicken PGCs of the instant invention are most closely related to the chicken ES cells taught by Pain. The PGCs of the instant invention were isolated from the dorsal aorta of stage 12-14 chicken embryos (page 19, line 7). The PGCs of 20 embryos were pooled, cultured in 0.25-0.5 pg/μl bFGF, 0.5625-1.125 pg/μl IGF, 4.0-8.0 pg/μl SCF and 0.00625-0.0125 U/μl LIF (page 21, lines 4 and 17) and transplanted into stage X chicken embryos such that germline chimeras that were not somatic cell chimeras were obtained. The range of amounts of growth factors in claim 3 appears to be 0.25-25 pg/μl bFGF, 0.5625-56.25 pg/μl IGF, 4-400 pg/μl SCF and 0.00625-0.625 U/μl LIF (see 112/2nd regarding the range and the use of "U/μl").

The avian ES of Pain were isolated from the blastoderm of stage 9-11 chicken embryos, cultured for more than 160 days in the presence of 10 ng/ml bFGF, 20 ng/ml IGF, 1% vol/vol SCF, 1% vol/vol LIF and injected into stage X embryos such that germline and somatic cell chimeras were obtained.

Thus, the avian cells disclosed and those taught by Pain were isolated from different stages (12-14 vs. 9-11), produced different chimeras (germline chimeras that were not somatic cell chimeras vs. germline and somatic cell chimeras) and were cultured in different amounts of bFGF, IGF, SCF and LIF. 10 ng/ml of bFGF and 20 ng/ml of IGF as taught by Pain are equivalent to 10 pg/μl and 20 pg/μl. Without evidence to the contrary, the amounts of bFGF and IGF taught by Pain are within the range of 4-400 pg/μl SCF and 0.00625-0.625 U/μl LIF. Therefore, while the actual amounts of bFGF, IGF, SCF and LIF used by applicants and by Pain differ, the amounts taught by Pain appear to be with the range claimed.

Claim Rejections - 35 USC § 112

1. Claims 9, 10 and 20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 9 and 10 are directed toward a method of culturing avian PGCs for prolonged periods using culture media comprising bFGF, IGF, SCF and LIF and transfecting the PGCs with

a nucleic acid sequence. Claim 20 is directed toward a transfected avian PGC cell line obtained by said method.

Claims 9 and 10 recite that the method requires transfecting the PGCs and claim 20 is directed toward a PGC transfected with a nucleic acid sequence. The only disclosed purpose for such a method or cell is to make a transgenic avian which is used to isolate exogenous proteins from the avian (page 8, line 22) or to change the phenotype of the bird (page 2, line 21). The state of the art at the time of filing was such that the phenotype of transgenic avians with an exogenous transgene was unpredictable. Wall (1996, Theriogenology, Vol. 45, pages 57-68) discloses the unpredictability of transgene behavior due to factors such as position effect and unidentified control elements resulting in a lack of transgene expression or variable expression (paragraph bridging pages 61-62). Thus, the level and the specificity of expression of a transgene is greatly dependent on the specific transgene construct used making the phenotype of transgenic animals unpredictable. The specification teaches that stably transfected PGCs have not been obtained (page 30, line 8). Neither the specification nor the art teach obtaining stably transfected PGCs or making transgenic birds using transfected PGCs. Therefore, the specification does not enable one of skill to use the method of transfecting PGCs or the transfected PGCs for the sole disclosed use of making transgenic avians because the specification does not enable changing the phenotype of the birds using transfected PGCs. Given the teachings in the specification taken with what was known in the art, it would have required one of skill undue experimentation to

determine how to obtain a stably transfected PGCs, the specific transgene construct required to make a transgenic avian such the phenotype of the avian was altered.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-10 and 18-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because the phrase "prolonged period of time" is not defined in the specification and does not have an art established definition such that the metes and bounds of the time period could be determined. Claims 2-10 and 18-20 are included in the rejection as they are dependent upon claim 1.

Claim 1 is indefinite because the phrase "U/μl" is indefinite. The specification does not define the units (U) of LIF and the term did not have an art recognized definition. Therefore, the metes and bounds of the amount of LIF encompassed by the claim cannot be determined. Claims 2-10 and 18-20 are included in the rejection as they are dependent upon claim 1.

The phrase "the minimal amounts" and "the maximal amounts" lack antecedent basis. The specification does not define the "maximal amounts of said growth factors range from about two times to one hundred times said minimum amounts." It is unclear how the amounts in claim 3

relate to the amounts in claim 2. The metes and bounds of the range being claimed cannot be determined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-8, 18 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Pain (7-25-96, Development, Vol. 122, pages 2339-2348, UnCover online at http://uncweb.carl.org/uncover/unchome.html) or in the alternative under 102 (a) as being anticipated by Pain (Pain et al., Aug. 1996, Development, Vol. 122, pages 2339-2348) and supported by Simkiss (Simkiss, 1994, MacLean, ed., Animals with novel genes, Transgenic birds, Cambridge Univ. Press, Cambridge England, NY, NY, pages 106-137).

Pain taught avian cells isolated from the blastoderm of a stage IX-XI chicken embryo were cultured for more than 160 days in the presence of 10 ng/ml bFGF, 20 ng/ml IGF, 1% vol/vol SCF, 1% vol/vol LIF (page 2340, col. 1, line 9; page 2340, col. 1, 4th and 5th full paragraphs; page 2345, col. 2, line 10). Simkiss taught that the blastoderm of stage X chicken embryos contain PGCs (page 111, Fig. 4.1, top panel). Therefore, Simkiss supports that the culture of

Pain inherently comprised PGCs. 10 ng/ml of bFGF and 20 ng/ml of IGF as taught by Pain are equivalent to 10 pg/μl and 20 pg/μl which is within the range of amounts in claim 3. Without evidence to the contrary, 1 % vol/vol SCF is inherently in the range of 4-400 pg/ml SCF. Without evidence to the contrary, 1% vol/vol LIF is inherently in the range of 0.00625-0.625 U/μl LIF. In addition, the amounts of growth factors are indefinite because the range is unclear and the term "U/μl" is not defined in the specification (see 112/2nd). Thus, Pain anticipates the claims.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1-6, 18 and 19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 and 10-12 of U.S. Patent No. 6,156,569, Dec. 5, 2000. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-5 and 10-12 of '569 are obvious species of claims 1-8, 18 and 19 in the instant application. Claims 1-5 and 10-12 of '569 are directed

toward a "pure population" of avian PGCs while the instant claims encompass any avian PGCs. The limitation of culturing the PGCs for at least 14 days in claims 1 of '569 is equivalent to claim 6 in the instant application.

5. Claims 1, 7 and 8 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 and 10-12 of U.S. Patent No. 6,156,569, Dec. 5, 2000 in view of Pain (Pain et al., 1996, Development, Vol. 122, pages 2239-23348).

The claims of '569 are directed toward culturing pure PGCs for at least 14 days. The claims do not recite the limitations of maintaining the cells for at least 25 days or 4 months. However, Pain taught culturing avian embryonic cells for at least 160 days (page 2345, col. 2). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the claimed invention in '569 to maintain the PGCs for at least 25 days or 4 months. One of ordinary skill would have been motivated to maintain the PGCs for at least 25 days or 4 months to increase the availability of the PGCs.

Claims 9, 10 and 20 appear to be free of the prior art of record because the prior art of record did not teach or suggest culturing avian PGCs in a culture medium comprising growth factors in amounts sufficient to maintain said PGCs for a prolonged period of time and transfecting the PGCs with a nucleic acid sequence.

Conclusion

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-0120.

Questions of formal matters can be directed to the patent analyst, Tracey Johnson, who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-2982.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 305-0196.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Deborah Clark, can be reached on (703) 305-4051.

The official fax number for this Group is (703) 308-4242.

Michael C. Wilson

MICHAEL C. WILSON
PATENT EXAMINER